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Diagnosis and management of chronic radiation enteritis

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INTRODUCTION

Injury to the intestines can occur following radiation therapy for cancer. It can affect both the large and small intestines, is often progressive, and may lead to a variety of clinical consequences depending upon the extent of the injury. It usually develops three or more months after radiation therapy. Chronic radiation enteritis is due to an obliterative arteritis that leads to intestinal ischemia, which can result in stricture, ulceration, fibrosis, and occasionally fistula formation. The physiologic consequences can include altered intestinal transit, reduced bile acid absorption, increased intestinal permeability, bacterial overgrowth, and lactose malabsorption. Clinical manifestations include nausea, vomiting, abdominal pain, diarrhea, weight loss, malnutrition, and bleeding (usually in patients with colonic involvement).

This topic review will focus on the diagnosis and management of chronic radiation injury to the small intestine and proximal colon. The pathogenesis, clinical manifestations, and risk factors for chronic radiation enteritis and other radiation-related gastrointestinal toxicities are discussed separately. (See "[Overview of gastrointestinal toxicity of radiation therapy](#)" and "[Radiation proctitis: Clinical manifestations, diagnosis, and management](#)".)

DIAGNOSIS

The diagnosis of chronic radiation enteritis is suspected in patients with nausea, vomiting, abdominal pain, diarrhea, or lower gastrointestinal bleeding three or more months after

completion of radiation therapy. The diagnosis is usually established by segmental bowel inflammation in regions of a known radiation field on imaging or by endoscopy and histology.

Diagnostic approach — Evaluation of a patient with suspected chronic radiation enteritis serves to exclude other causes of etiologies, establish the diagnosis of chronic radiation, and determine the extent of the disease.

- The patient's prior radiation treatment should be reviewed to determine the cumulative dose, dose per fraction, proximity of sensitive tissues and organs, and other cancer treatments (eg, abdominal surgery, concurrent chemotherapy) that can increase the risk of radiation enteritis. This may help to determine which intestinal segments may have received excessive radiation exposure, which can then be correlated with the radiologic findings and the clinical presentation.
- In patients with abdominal pain, nausea, and vomiting, we begin evaluation with an abdominal computed tomography (CT) or magnetic resonance (MR) enterography and an upper gastrointestinal endoscopy. In patients with diarrhea or hematochezia, we perform a colonoscopy.
- Patients with persistent symptoms and negative initial evaluation should be reassessed, and both imaging (CT/MR enterography) and endoscopy (upper endoscopy and colonoscopy) should be performed if not performed as part of the initial evaluation.
- Patients with diarrhea, abdominal pain, or bloating should also undergo breath testing for bacterial overgrowth.
- Additional evaluation with capsule endoscopy or enterography should be performed only in patients with no evidence of radiation enteritis on endoscopy and imaging and in whom there is strong clinical suspicion for radiation enteritis causing small bowel bleeding (formerly obscure gastrointestinal bleeding). (See ['Additional evaluation'](#) below and ["Wireless video capsule endoscopy"](#), section on ['Risks'](#).)

Endoscopy and biopsy — Mucosal features consistent with radiation injury include pallor with friability and telangiectasias, which can be multiple, large, and serpiginous; these changes tend to be continuous. Histologic findings of radiation enteritis include diffuse collagen deposition with mucosal and serosal thickening, inflammatory cell infiltrates, vascular sclerosis, and occlusive vasculitis.

Imaging — CT/MR enterography findings include segmental inflammation. These include bowel thickening, mucosal hyperenhancement, mesenteric stranding, and luminal stricturing. In the

later stages, stenotic segments and ultimate small bowel obstruction can occur as a result of fibrosis.

CT/MR enteroclysis is an alternative to enterography in patients who cannot tolerate oral contrast. Enteroclysis involves installation of contrast into the intestine using a nasoenteric tube. Vomiting, which is sometimes associated with enterography, is avoided in enteroclysis by control of infusion rates fluoroscopically. For identifying low-grade or intermittent obstruction, CT enteroclysis has a reported sensitivity and specificity of approximately 88 and 82 percent, respectively [1,2]. Studies suggest the results are comparable to and possibly more sensitive than CT enteroclysis [3]. However, only small numbers of patients have been studied, and the technique is not yet widely available. Upper gastrointestinal series with small bowel follow-through, although useful for evaluating the extent of disease, are not as sensitive as enteroclysis or enterography and are therefore rarely performed [4].

Additional evaluation

- **Breath test for small intestinal bacterial overgrowth** – Specific testing for bacterial overgrowth is preferable to empiric therapy in patients with unexplained diarrhea, abdominal pain, or bloating. A major drawback to empiric therapy is that treatment may require more than one antibiotic and repeated and sometimes cyclic treatment. Because antibiotics may be associated with adverse effects, some of which may mimic symptoms of bacterial overgrowth (such as diarrhea and abdominal discomfort), establishing a firm diagnosis is important. This can usually be accomplished with a breath test.
- **Capsule endoscopy** – There is little published experience with capsule endoscopy specifically for diagnosing radiation enteritis, although there is some clinical experience ([picture 1](#) and [picture 2](#)) [5]. Capsule endoscopy should not be performed in patients with evidence of an intestinal stricture on CT/MR enterography. A patency capsule should be considered prior to capsule endoscopy in order to exclude subtle, yet important, luminal narrowing(s) in which a video capsule may become lodged. (See "[Evaluation of suspected small bowel bleeding \(formerly obscure gastrointestinal bleeding\)](#)", section on '[Wireless video capsule endoscopy](#)'.)
- **Enteroscopy** – The role of deep small bowel enteroscopy is limited to patients with small bowel bleeding [6]. This is discussed in detail, separately. (See "[Evaluation of suspected small bowel bleeding \(formerly obscure gastrointestinal bleeding\)](#)", section on '[Deep small bowel enteroscopy](#)'.)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of chronic radiation enteritis varies based on the clinical presentation. The main differential diagnoses to consider in patients with diarrhea and abdominal pain include infection, new/recurrent neoplasia, small intestinal bacterial overgrowth, pancreatic insufficiency, and new onset of inflammatory bowel disease. (See ["Approach to the adult with chronic diarrhea in resource-abundant settings"](#) and ["Causes of abdominal pain in adults"](#) and ["Evaluation of the adult with abdominal pain"](#).)

MANAGEMENT

Approach to management — Management of chronic radiation enteritis is based on treating the predominant symptoms. In patients with diarrhea, this consists of dietary modification and, based on the severity of diarrhea, antidiarrheal agents and bile acid-binding resins. Patients with diarrhea, bloating, and abdominal pain who have evidence of small intestinal bacterial overgrowth should be treated with antibiotics.

Patients with intermittent obstructive symptoms should be advised a low-residue diet. Surgery in patients with chronic radiation enteritis should be performed selectively and only for persistent bowel obstruction, fistula, or gastrointestinal bleeding that fails to resolve with medical management. (See ["Management of small bowel obstruction in adults"](#), section on 'Indications for immediate surgery' and ["Enterocutaneous and enteroatmospheric fistulas"](#), section on 'Timing of surgery' and ["Approach to acute lower gastrointestinal bleeding in adults"](#) and ["Approach to acute upper gastrointestinal bleeding in adults"](#).)

Dietary modification — There does not appear to be a clear-cut diet that reliably alleviates all symptoms of chronic radiation enteritis. However, patients should be instructed to avoid foods that are high in fiber, such as fruits, vegetables, and whole grains. A high-fiber diet may worsen diarrhea and urgency [7]. A recent meta-analysis of randomized controlled trials suggested that prophylactic probiotics may be useful for the treatment of radiation-induced diarrhea [8].

Patients with lactose intolerance should be advised to restrict but not eliminate dietary lactose. Some patients who develop lactose intolerance due to bacterial overgrowth may improve following antibiotic treatment. (See ["Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management"](#), section on 'Management'.)

The use of total [parenteral nutrition](#) in patients with chronic radiation enteritis is limited to those with severe malnutrition due to malabsorption or short bowel syndrome due to small

bowel resection [9-12]. (See 'Surgery' below and "[Management of short bowel syndrome in adults](#)", section on 'Management in adaptation phase'.)

Antidiarrheal agents — Antidiarrheal agents (eg, [loperamide](#)) can help improve diarrhea, although they should not be used in patients with suspected small or large bowel obstruction. (See "[Etiologies, clinical manifestations, and diagnosis of mechanical small bowel obstruction in adults](#)", section on 'Clinical presentations'.)

The efficacy of [loperamide](#) was evaluated in a crossover trial involving 18 patients with diarrhea due to radiation enteritis who were randomly assigned to loperamide or placebo for 14 days, separated by a 14-day washout period [13]. Loperamide was associated with a significant reduction in the frequency of bowel movements, slower intestinal transit, and improvement in the absorption of bile acids.

Bile acid sequestrants — In patients with persistent diarrhea despite antidiarrheals, we use bile acid sequestrants (eg, [cholestyramine](#), [colestipol](#), [colesevelam](#)). However, their use is limited by associated gastrointestinal side effects including bloating, flatulence, abdominal discomfort, and constipation. The rationale for the use of bile acid sequestrants is that the prevalence of bile salt malabsorption is estimated to be as high as 50 percent in patients with a history of pelvic radiotherapy [14].

Antibiotics — Antibiotics can reduce symptoms in patients with evidence of small intestinal bacterial overgrowth. (See "[Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis](#)" and "[Small intestinal bacterial overgrowth: Management](#)".)

Surgery — Surgery for radiation enteritis should be avoided if possible because of several inherent difficulties in operating on patients with chronic radiation injury [15]:

- Diffuse fibrosis and adhesions between bowel loops can make resection technically challenging.
- The risk of a leak is high when creating an anastomosis between irradiated tissues [16]. Furthermore, it can be difficult to distinguish healthy tissue from irradiated tissue by gross inspection alone; intraoperative endoscopy may be helpful in this setting, but experienced is limited [17].
- Extensive resection may be required, potentially leading to short bowel syndrome. (See "[Pathophysiology of short bowel syndrome](#)" and "[Management of short bowel syndrome in adults](#)".)

Surgical approaches to radiation enteritis vary with each patient. In general, surgical techniques include bowel resection, intestinal bypass, and strictureplasty. Because strictureplasty conserves intestinal length, it is useful in treating patients with limited intestinal reserve who present with intestinal stricture(s) [18]. Experience with small bowel transplantation in patients with chronic radiation enteritis is limited, and its role is still being evaluated [19,20]. (See "[Overview of intestinal and multivisceral transplantation](#)", section on 'Indications' and "[Surgical approach to radiation enteritis](#)".)

Other — Other therapies have been evaluated in patients with radiation enteritis, but evidence to support their use is limited.

- **Hyperbaric oxygen (HBO)** – HBO therapy has been associated with improved outcomes in patients with radiation enteritis in some observational studies, but results have been conflicting [21]. HBO is also expensive and not widely available outside of centers specializing in this approach. (See "[Hyperbaric oxygen therapy](#)".)
- **Nerve block** – Splanchnic and mesenteric arterial block has been used in addition to reduce patient's symptoms [22].

PROGNOSIS

Prognosis is variable since the disease is progressive. Early mortality is usually due to cancer recurrence. Five-year survival is approximately 70 percent in those without cancer recurrence, although many patients continue to have troubling digestive symptoms for the remainder of their lives. Despite attempts at medical management, approximately one-third of patients progress to the point where surgery is required [23]. Surgical mortality rates range from 0 to 35 percent, and many patients require more than one laparotomy [16,23-26].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Radiation-induced gastrointestinal toxicity](#)".)

SUMMARY AND RECOMMENDATIONS

- Chronic radiation enteritis usually develops three or more months after radiation therapy. Chronic radiation enteritis is due to an obliterative arteritis that leads to intestinal ischemia, which can result in stricture, ulceration, fibrosis, and occasionally fistula formation. The physiologic consequences can include altered intestinal transit, reduced bile acid absorption, increased intestinal permeability, small intestinal bacterial overgrowth, and lactose malabsorption. Clinical manifestations include nausea, vomiting, abdominal pain, diarrhea, weight loss, malnutrition, and bleeding. (See ['Introduction'](#) above and ["Overview of gastrointestinal toxicity of radiation therapy"](#), section on ['Enteritis'](#).)
- The diagnosis of chronic radiation enteritis is suspected in patients with nausea, vomiting, abdominal pain, diarrhea, or gastrointestinal bleeding three or more months after completion of radiation therapy. The diagnosis is usually established by segmental bowel inflammation in regions of a known radiation field on imaging or by endoscopy and histology. (See ['Diagnosis'](#) above.)
- In patients with abdominal pain, nausea, and vomiting, we begin evaluation with an abdominal computed tomography (CT) or magnetic resonance (MR) enterography and an upper gastrointestinal endoscopy. In patients with diarrhea or hematochezia, we perform a colonoscopy. Patients with persistent symptoms and negative initial evaluation should be reassessed, and both imaging (CT/MR enterography) and endoscopy (upper endoscopy and colonoscopy) should be performed if not performed as part of the initial evaluation. Patients with diarrhea, abdominal pain, or bloating should also undergo breath testing for small intestinal bacterial overgrowth. (See ['Diagnostic approach'](#) above.)
- Additional evaluation with capsule endoscopy or enterography should be performed only in patients with no evidence of radiation enteritis on endoscopy and imaging and in whom there is strong clinical suspicion for radiation enteritis causing small bowel bleeding (formerly known as obscure gastrointestinal bleeding). (See ['Additional evaluation'](#) above and ["Evaluation of suspected small bowel bleeding \(formerly obscure gastrointestinal bleeding\)"](#), section on ['Wireless video capsule endoscopy'](#).)
- Management of chronic radiation enteritis is based on treating the predominant symptoms. In patients with diarrhea, this consists of dietary modification and, based on the severity of diarrhea, antidiarrheal agents and bile acid-binding sequestrants. Patients with diarrhea, bloating, and abdominal pain who have evidence of small intestinal bacterial overgrowth should be treated with antibiotics. (See ["Small intestinal bacterial overgrowth: Management"](#), section on ['Antibiotic therapy'](#).)

Patients with intermittent obstructive symptoms may benefit from a low-residue diet, although dietary tolerance is variable. Surgery in patients with chronic radiation enteritis should be performed selectively and only for persistent bowel obstruction, fistula, or gastrointestinal bleeding that fails to resolve with medical management. (See '[Surgery](#)' above.)

- Prognosis is variable since the disease is progressive. Early mortality is usually due to cancer recurrence. Five-year survival is approximately 70 percent in those without cancer recurrence, although many patients continue to have troubling digestive symptoms for the remainder of their lives. Despite attempts at medical management, approximately one-third of patients progress to the point where surgery is required. Surgical mortality rates range from 0 to 35 percent, and many patients require more than one laparotomy. (See '[Prognosis](#)' above.)

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GRAPHICS

Radiation enteritis



Abnormal jejunal villi and lacteals secondary to radiation enteritis as seen during capsule endoscopy.

Courtesy of Ingram Roberts MD.

Graphic 75475 Version 1.0

Radiation enteritis



Capsule endoscopy showing a jejunal stricture secondary to radiation enteritis.

Courtesy of Ingram Roberts MD.

Graphic 53206 Version 1.0

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